



Figure 1: Sedation Model

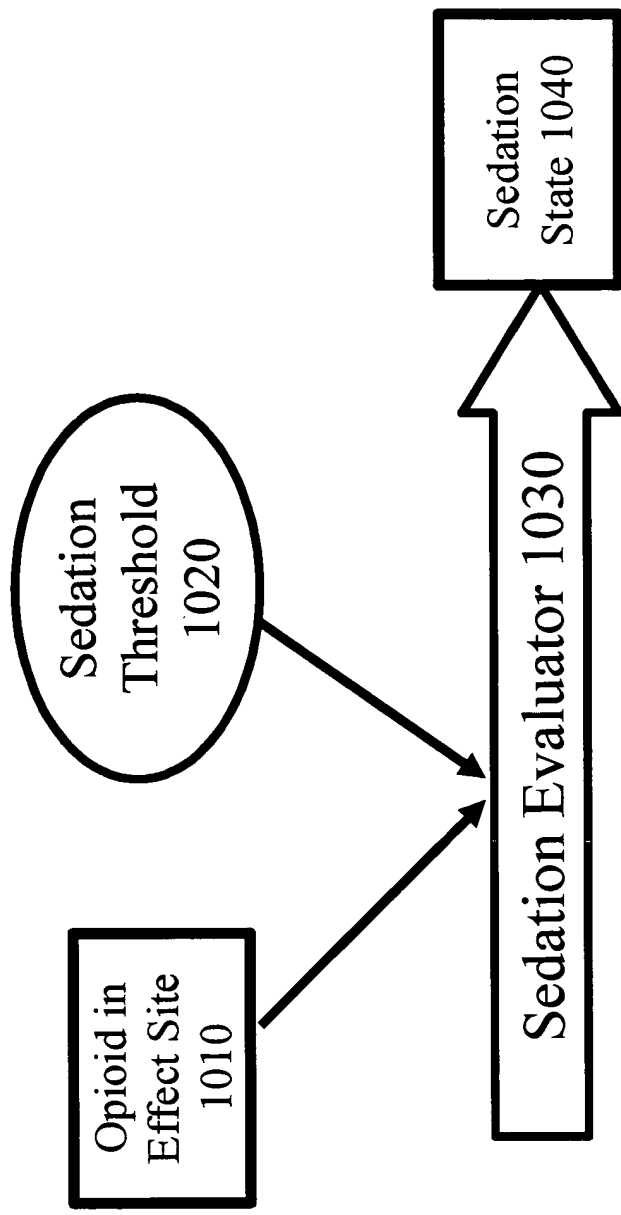


Figure 2: Ventilatory Depression Model

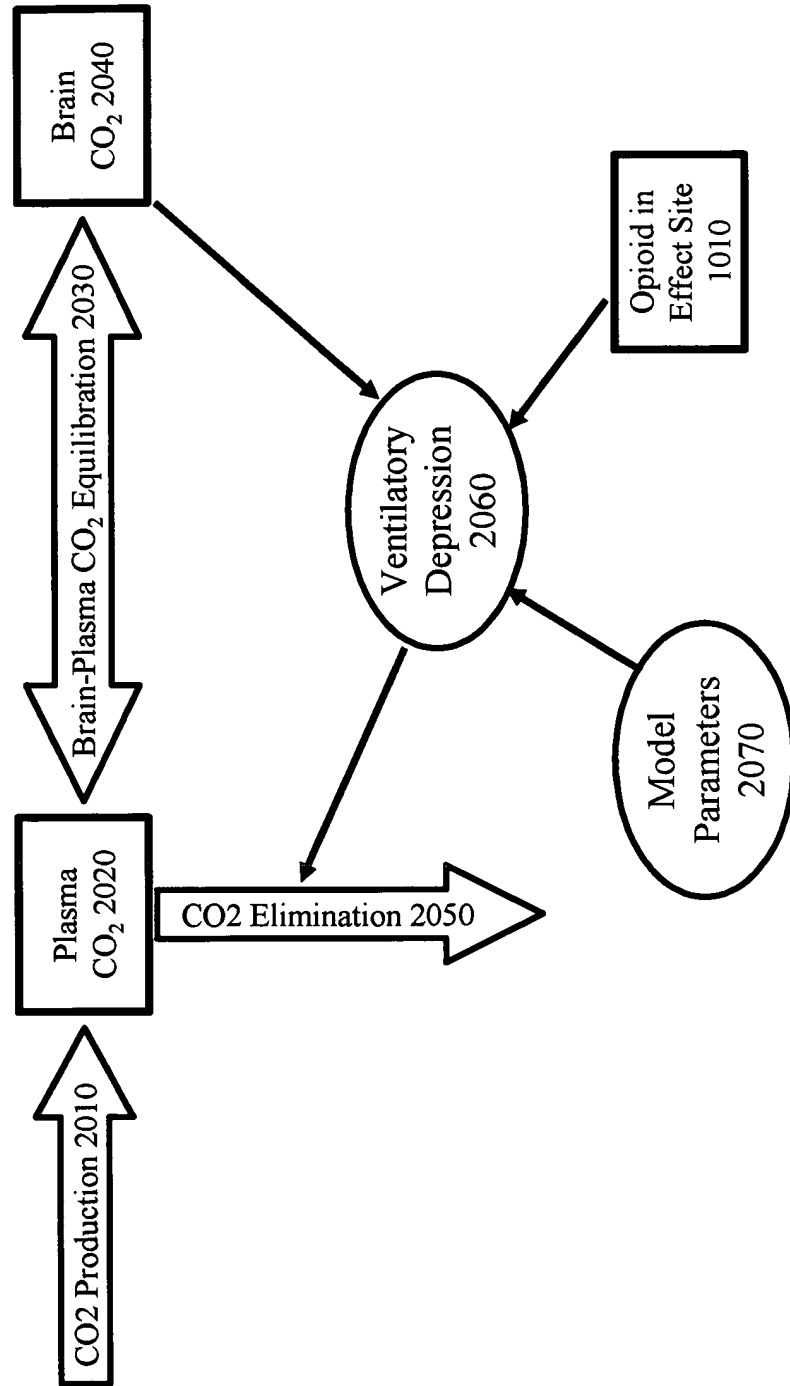


Figure 3: Device Model

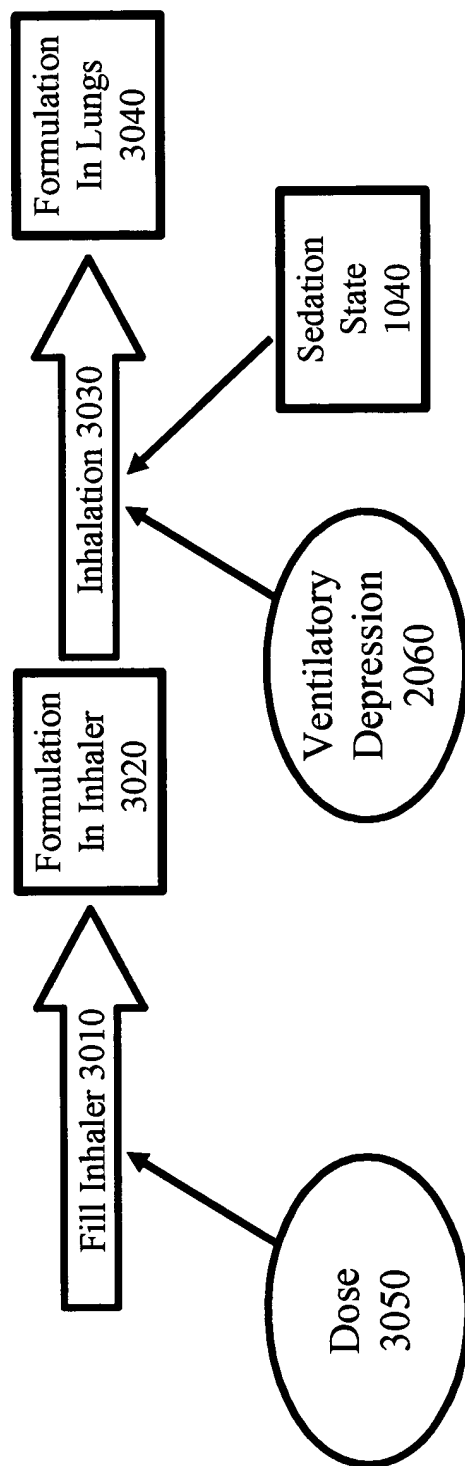


Figure 4: Pharmacokinetic Model

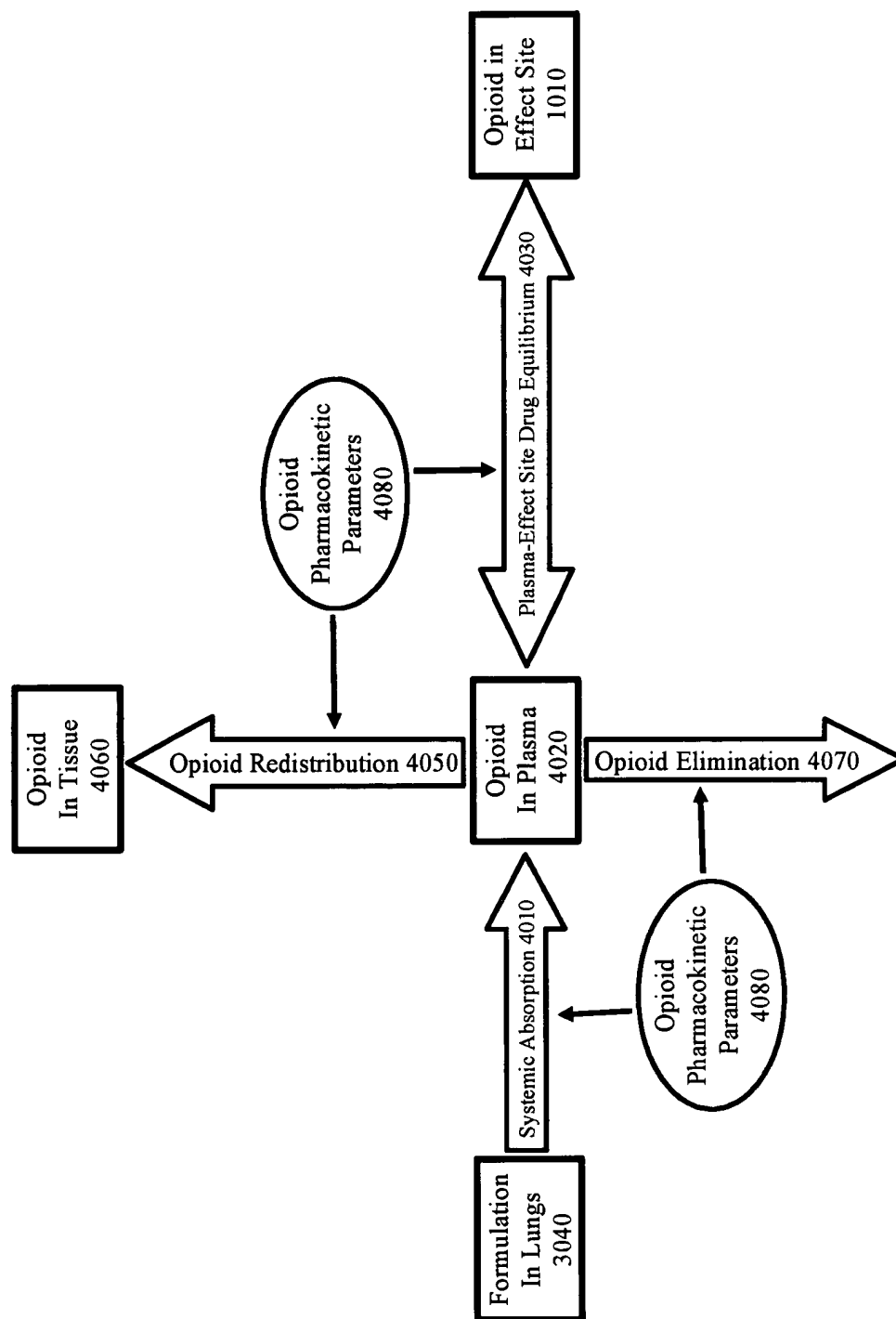


Figure 5A

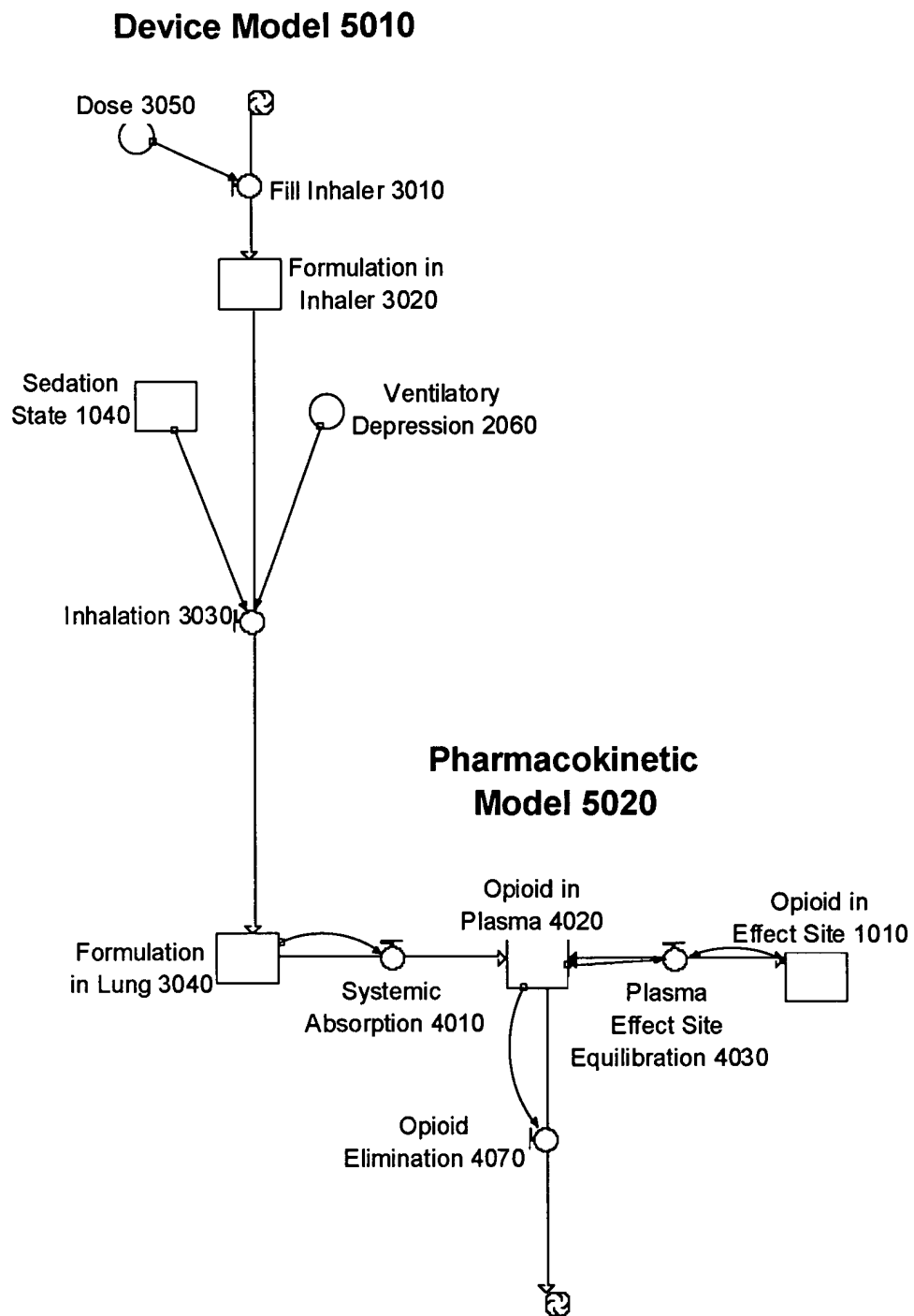
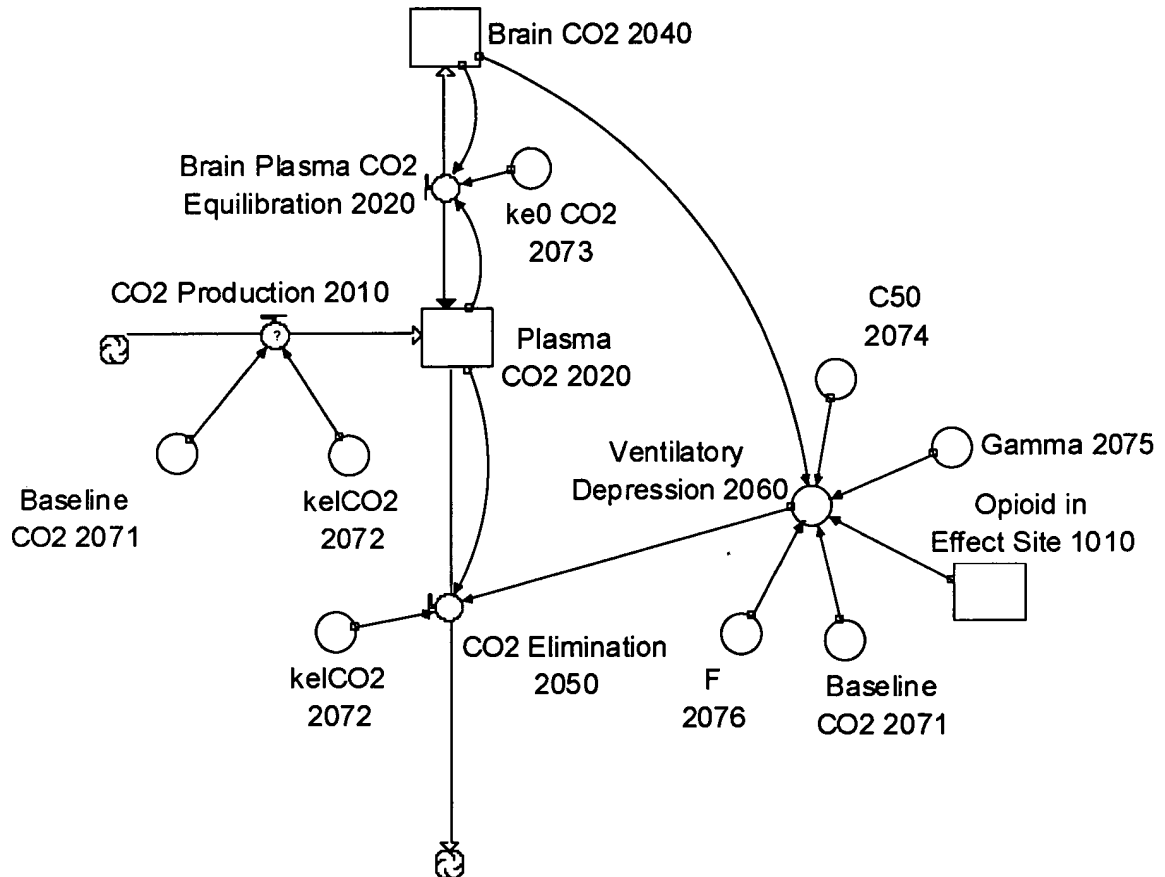


Figure 5B

Ventilatory Depression Model 5030



Sedation Model 5040

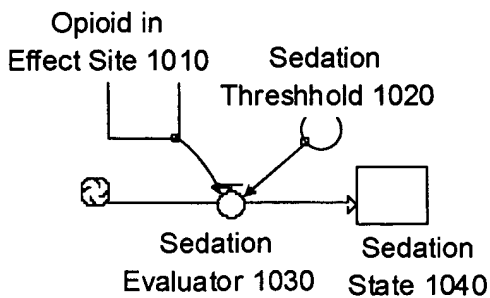


Figure 6

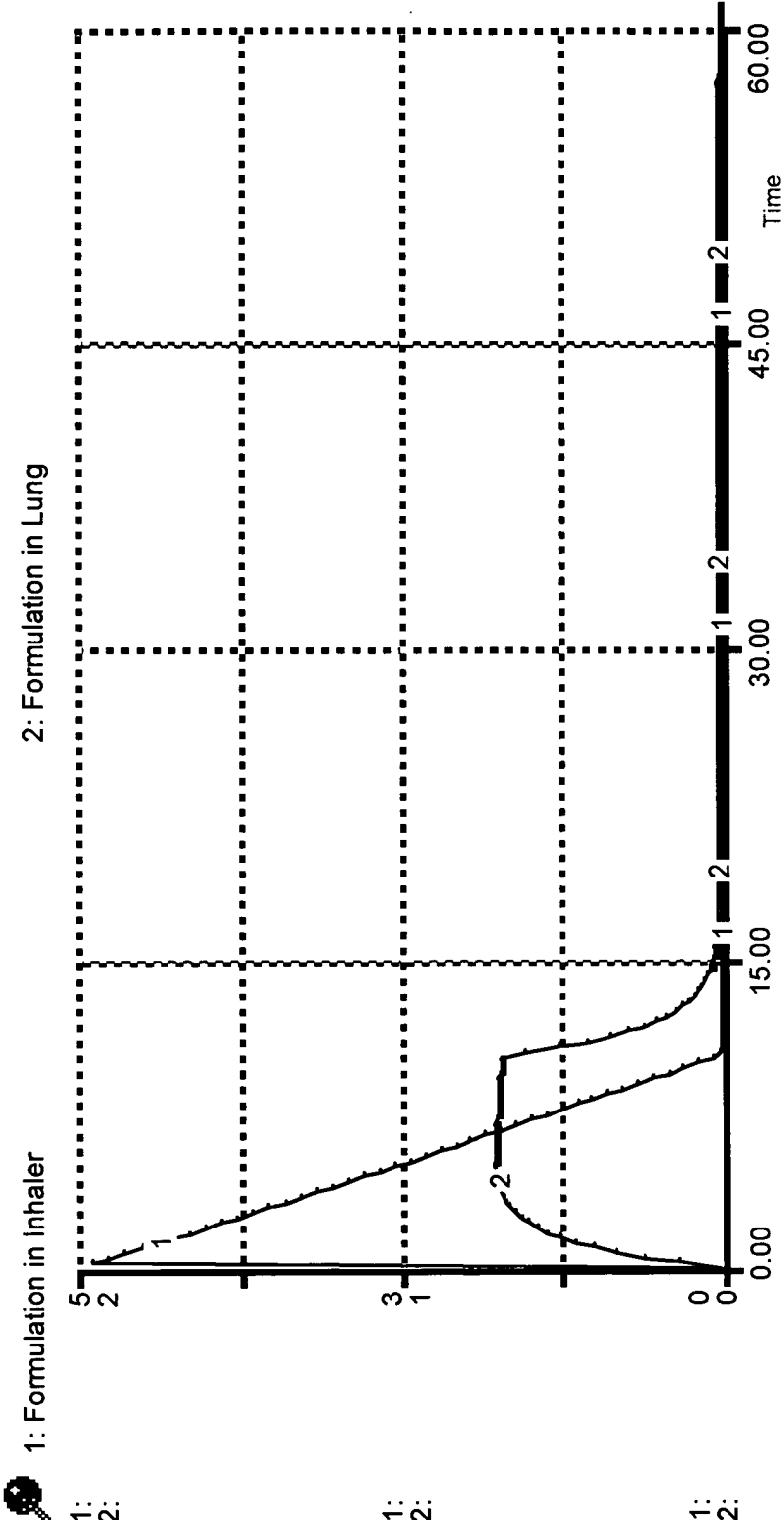


Figure 7

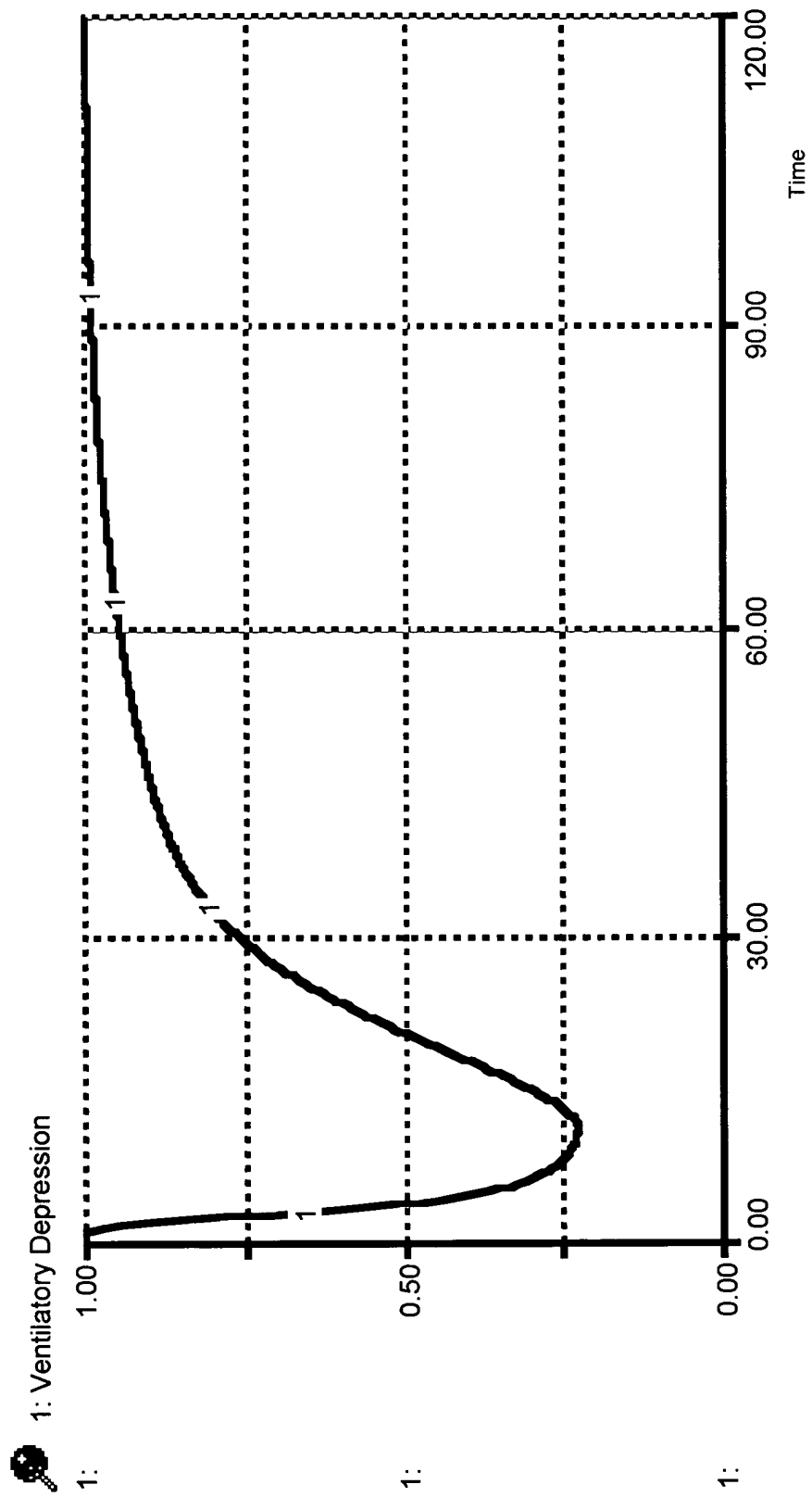


Figure 8

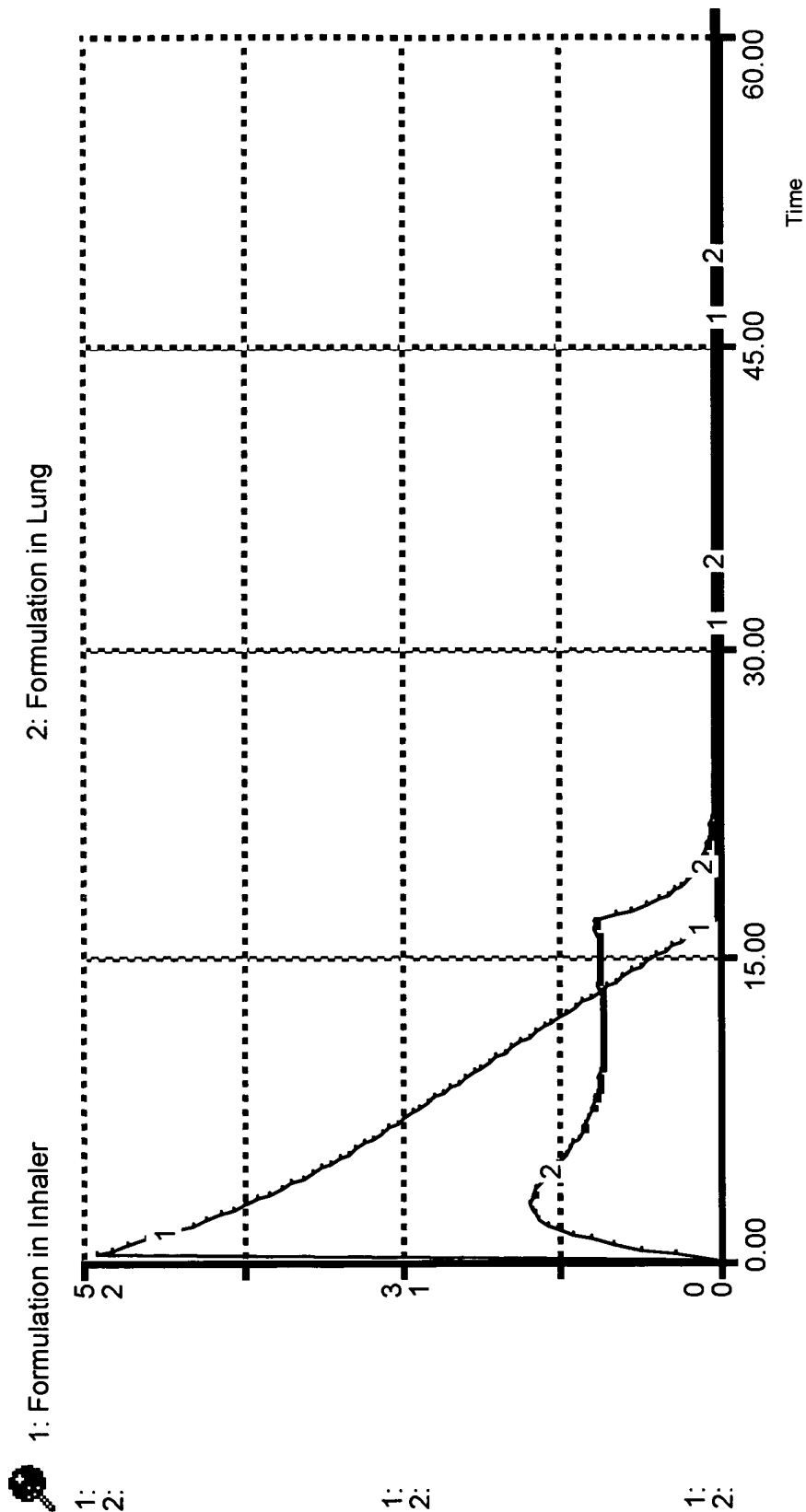


Figure 9

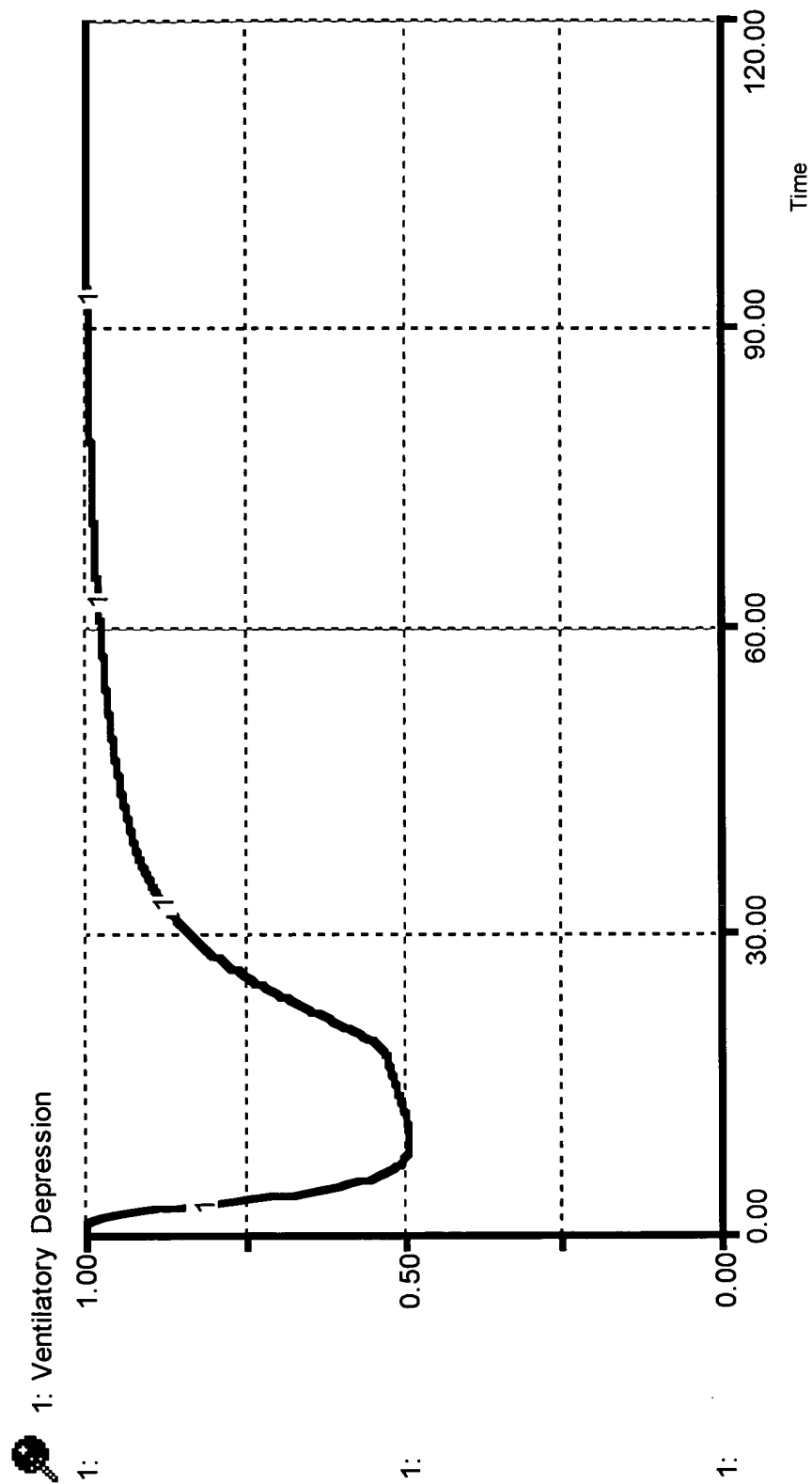


Figure 10

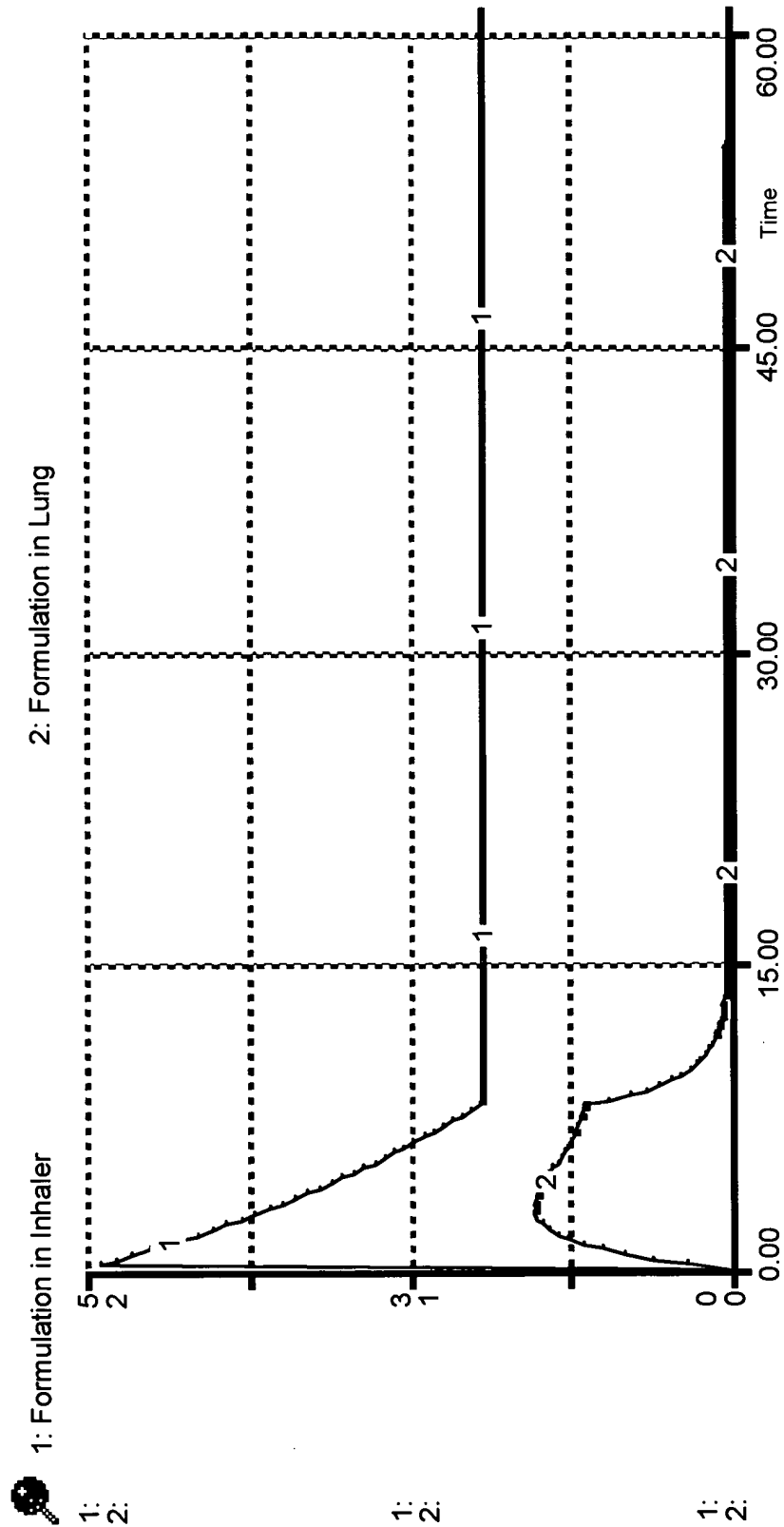


Figure 11

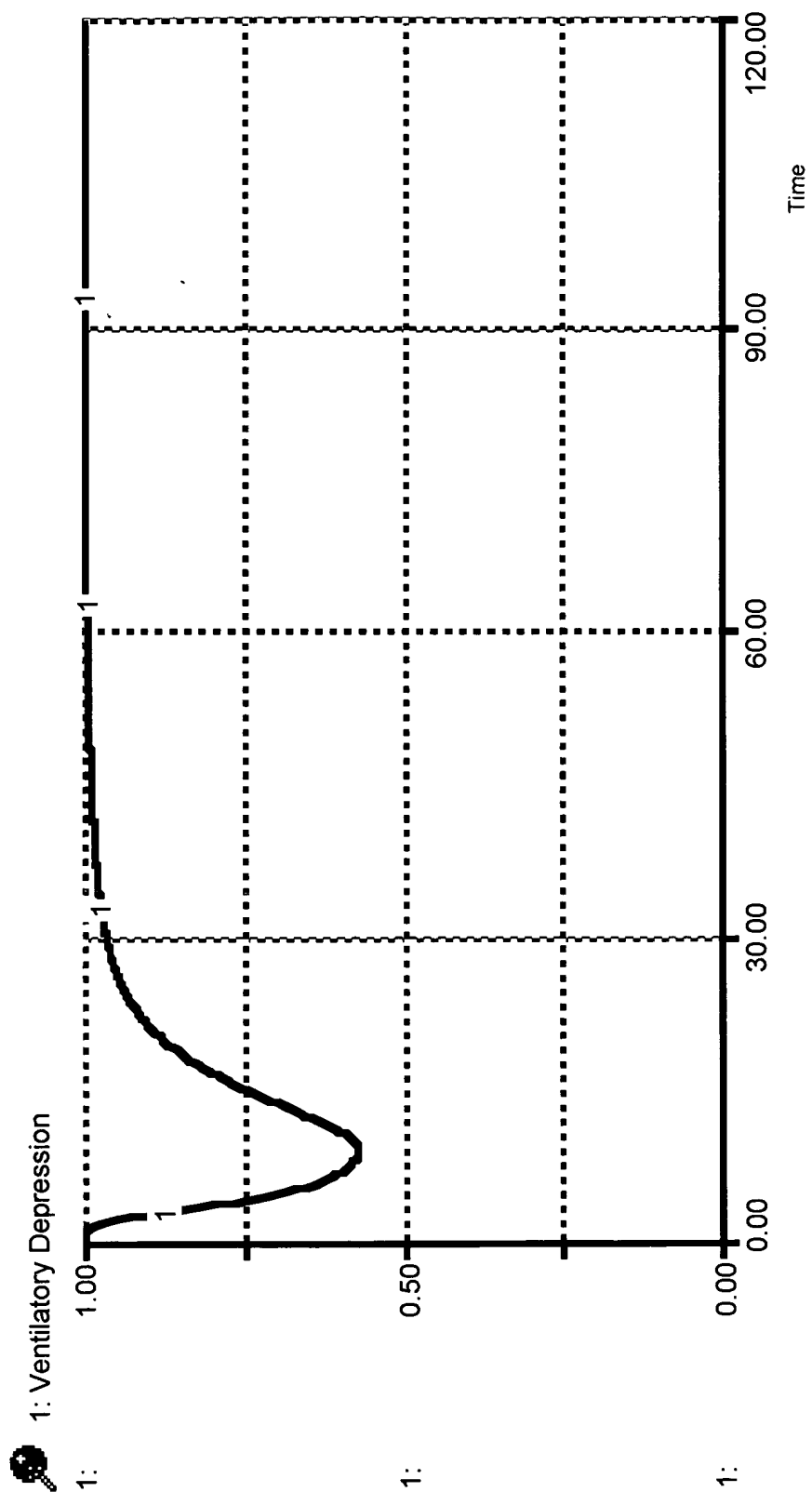


Figure 12: Two Opioid Model

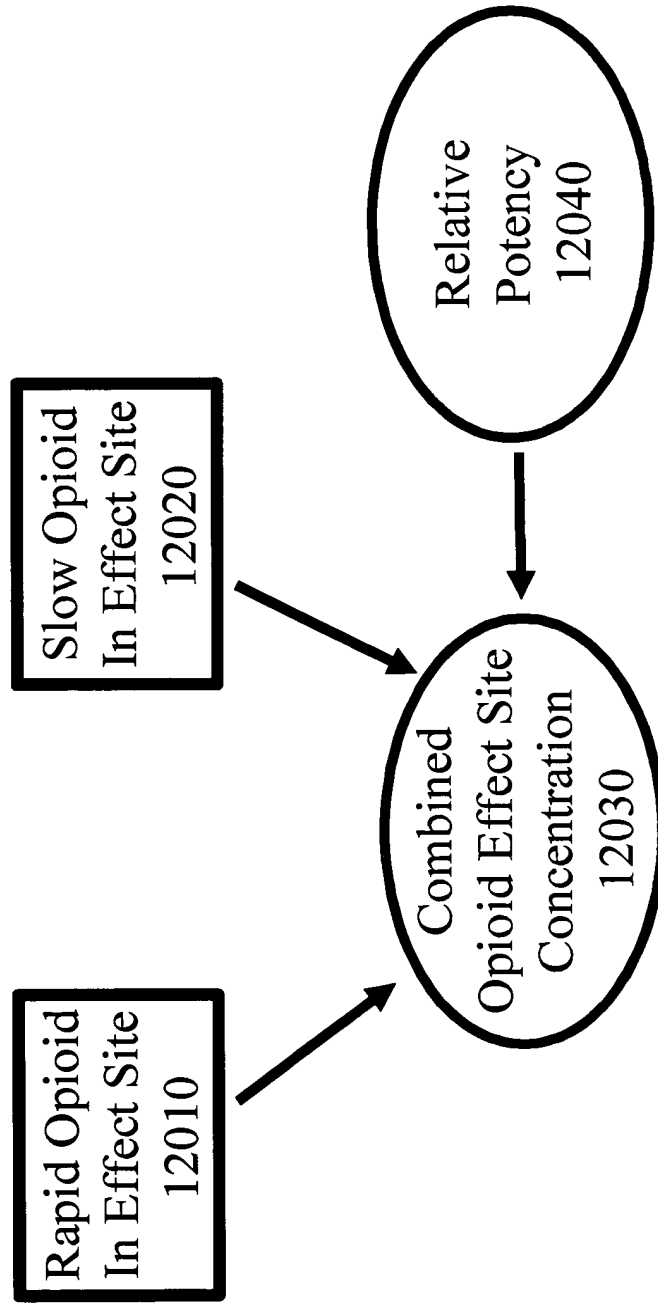


Figure 13A: The elements of the invention, wherein two opioids are administered through inhalation.

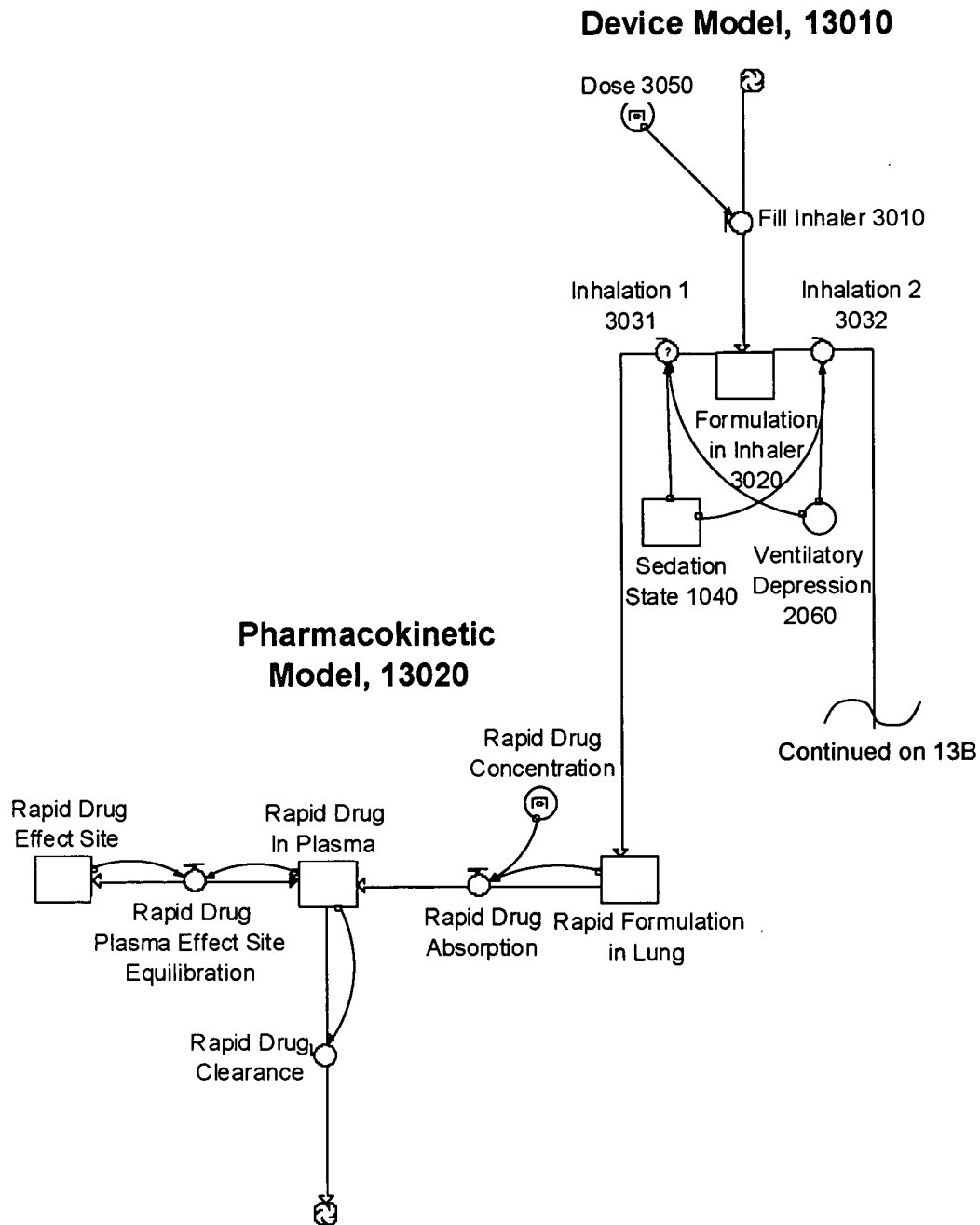


Figure 13B The elements of the invention, wherein two opioids are administered through inhalation.

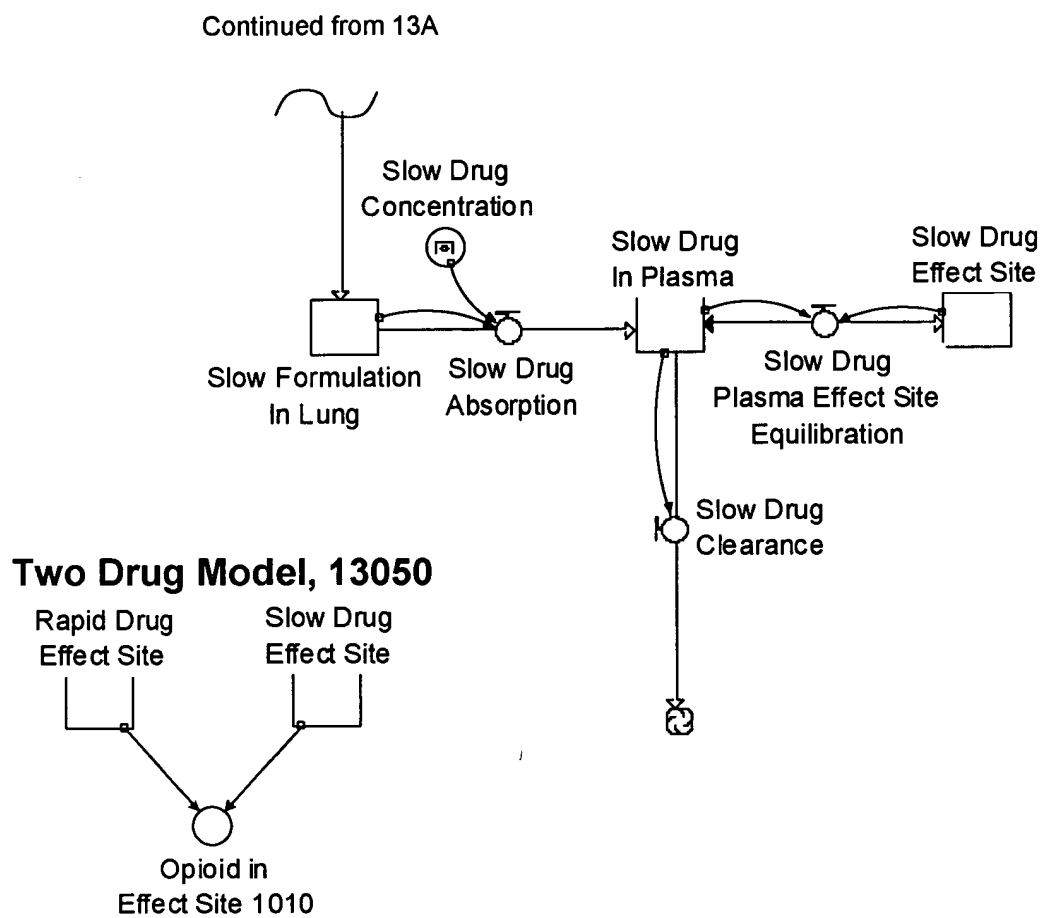


Figure 13C The elements of the invention, wherein two opioids are administered through inhalation.

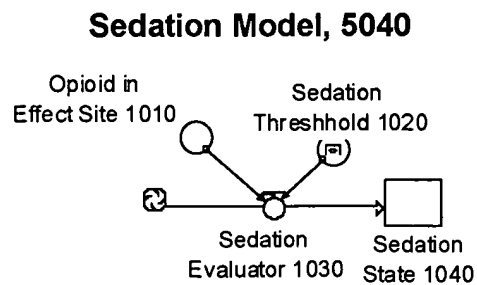
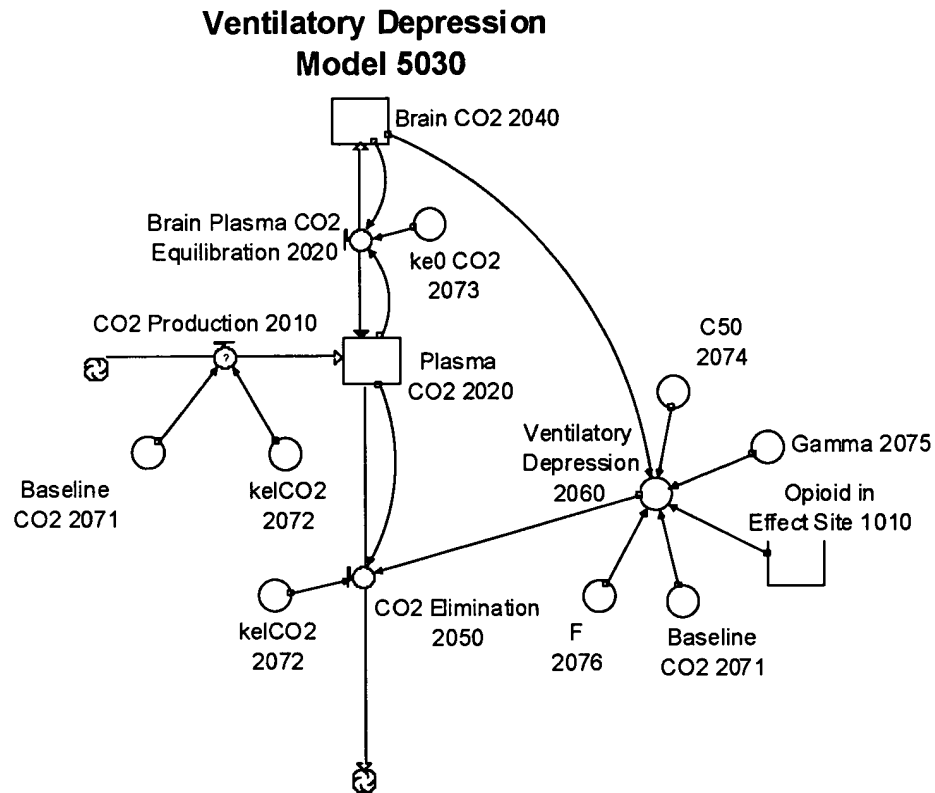


Figure 14: Drug in inhaler and lung in the presence of opioid-induced ventilatory depression and sedation for the two opioid model.

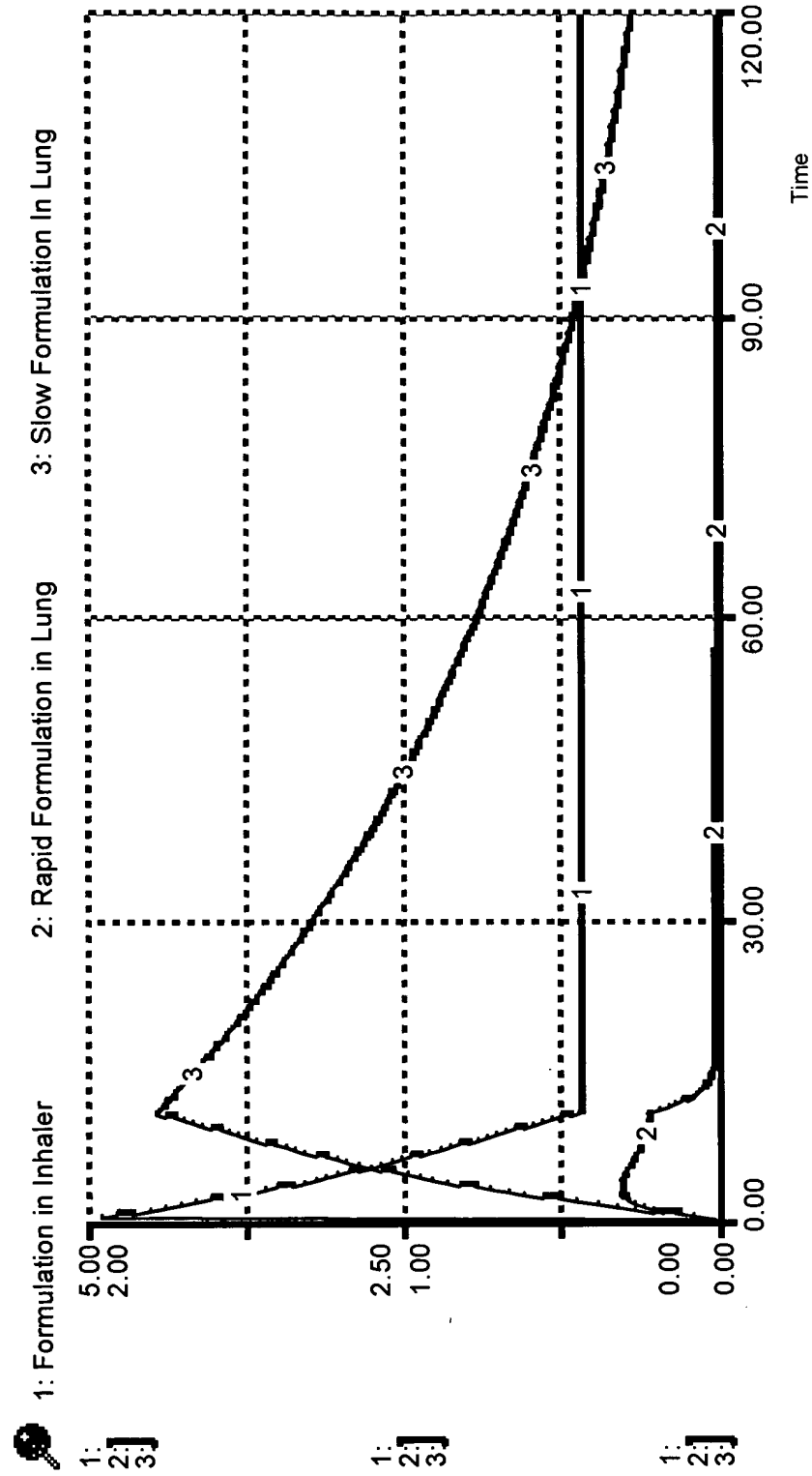


Figure 15: The rapidly acting opioid concentration in the effect site, the slowly acting opioid concentration in the effect site, and the combined concentration of opioid at the effect site, during two opioid administration with the device.

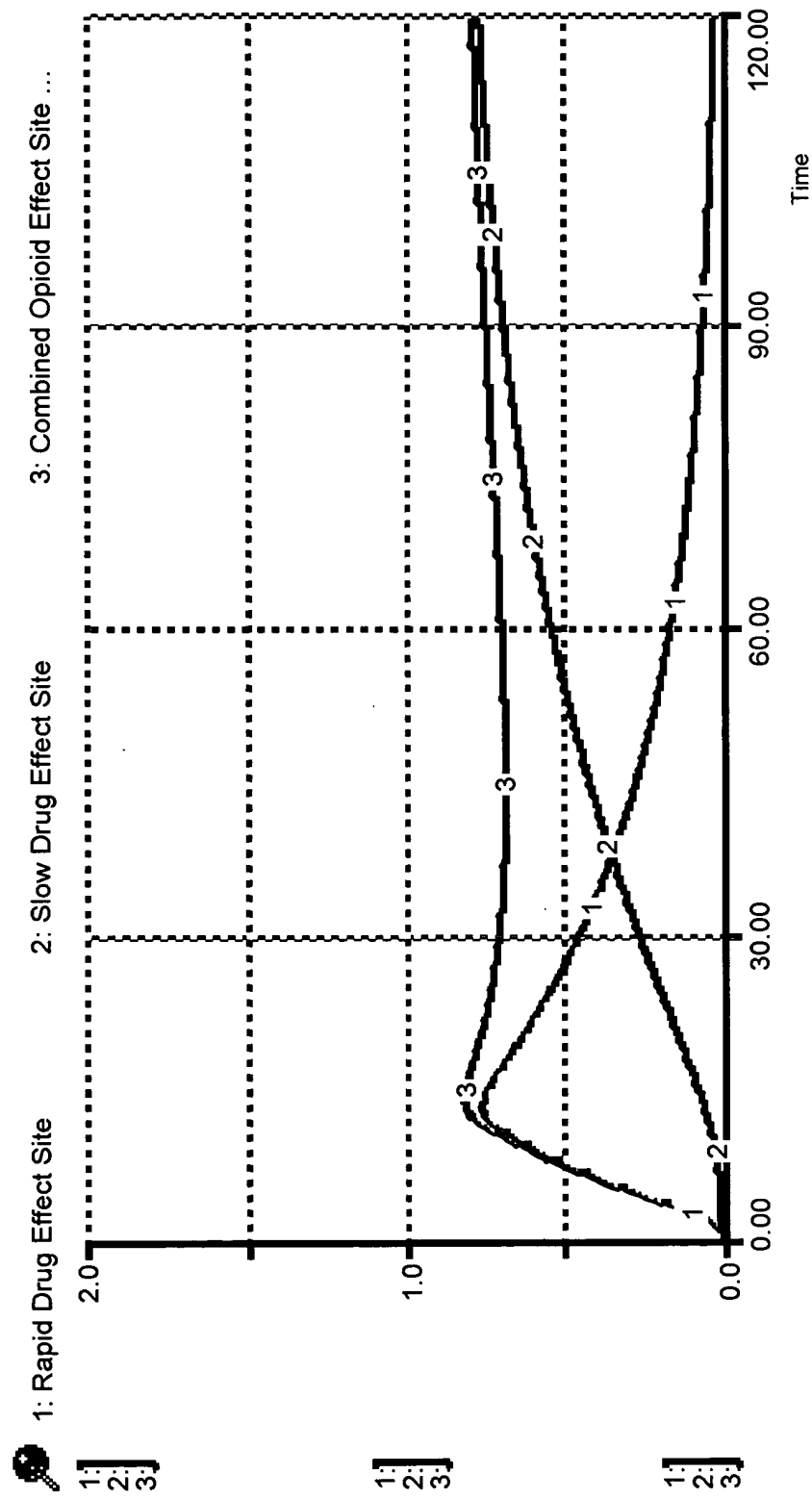


Figure 16: Ventilatory depression in the presence of self-limitation of opioid delivery from ventilatory depression and sedation with the two-opioid delivery system.

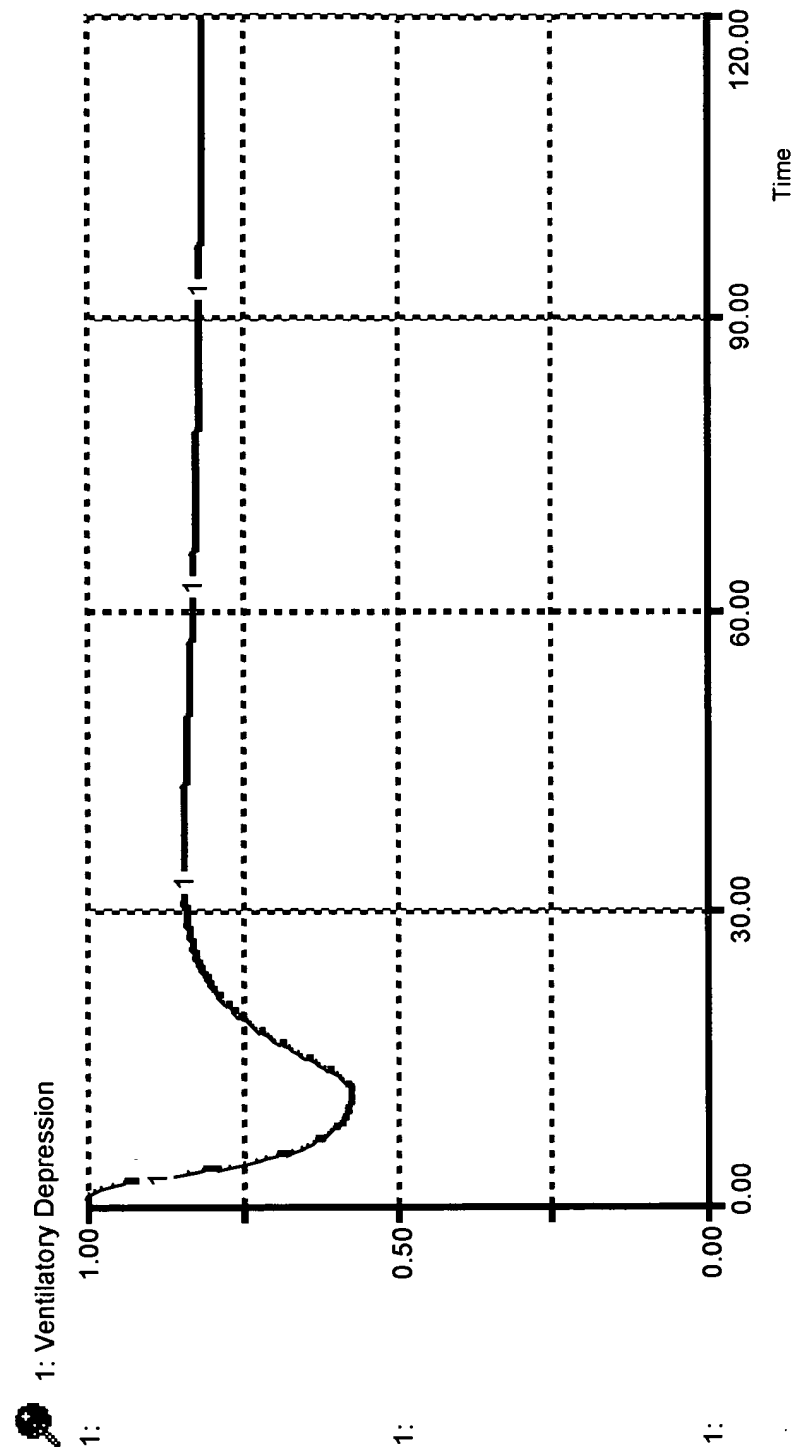
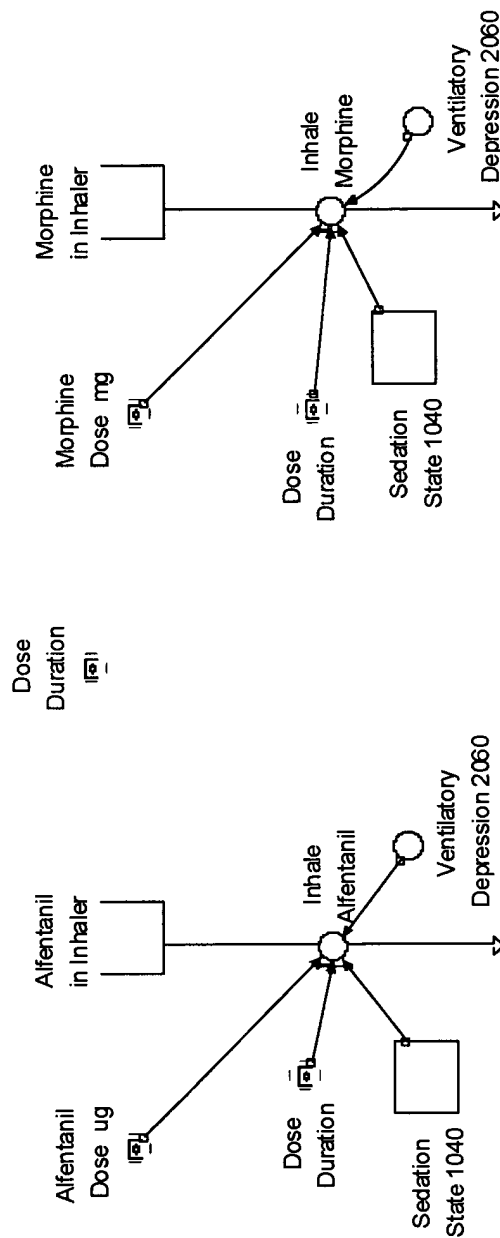
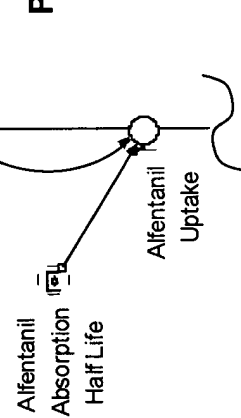


Figure 17A: The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

Device Model, 17010



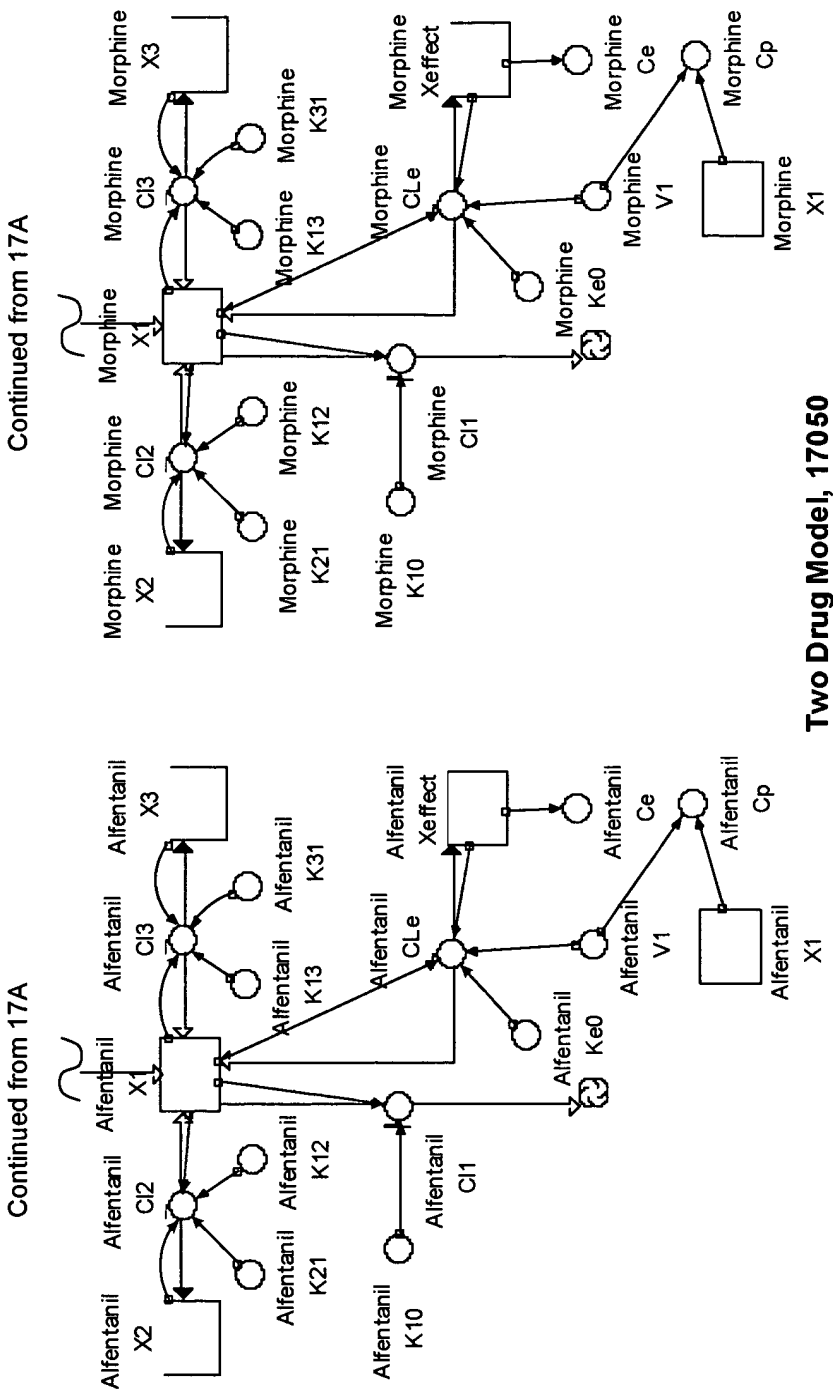
Pharmacokinetic Model, 17020



Continued on 17B

Continued on 17B

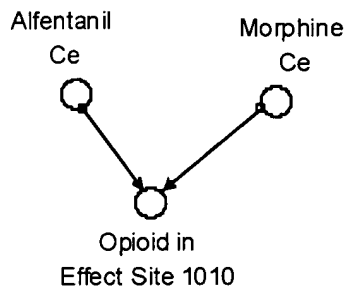
Figure 17B: The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.



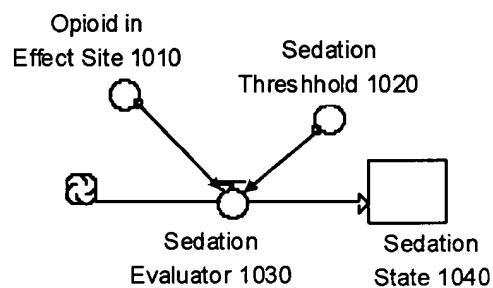
Two Drug Model, 17050

Figure 17C: The elements of the invention, wherein two opioids are administered through inhalation, and the rapidly acting opioid is alfentanil, and the slowly acting opioid is morphine.

Two Drug Model, 17050



Sedation Model 5040



Ventilatory Depression Model 5030

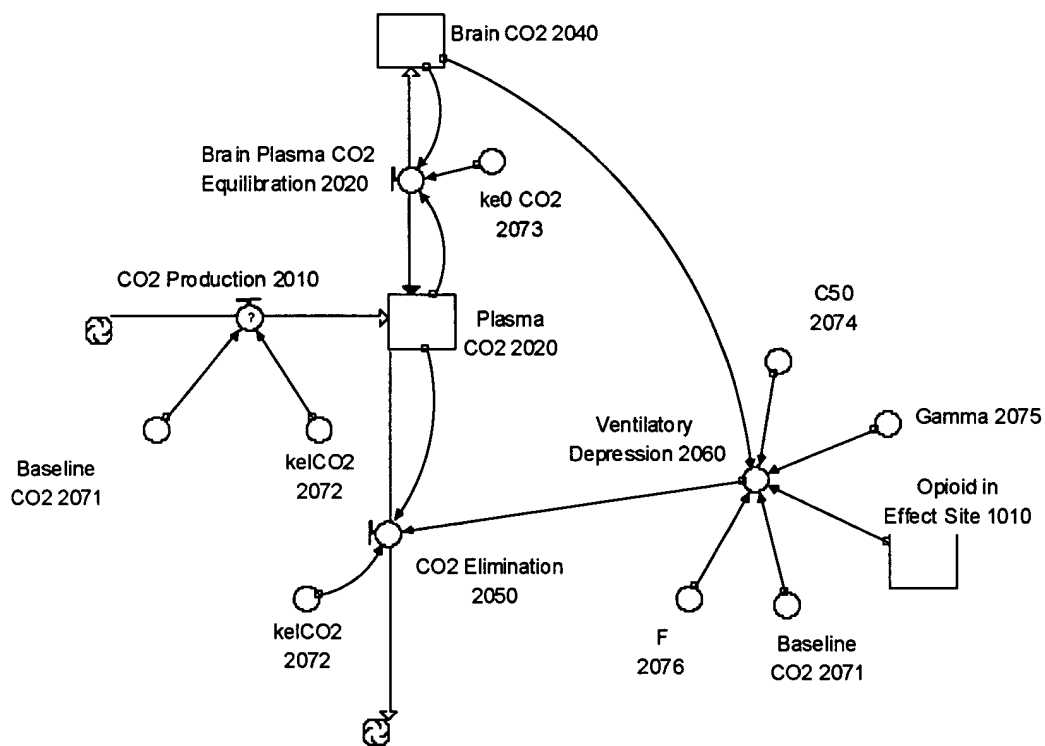


Figure 18: Alfentanil, morphine, and combined opioid effect site concentrations.

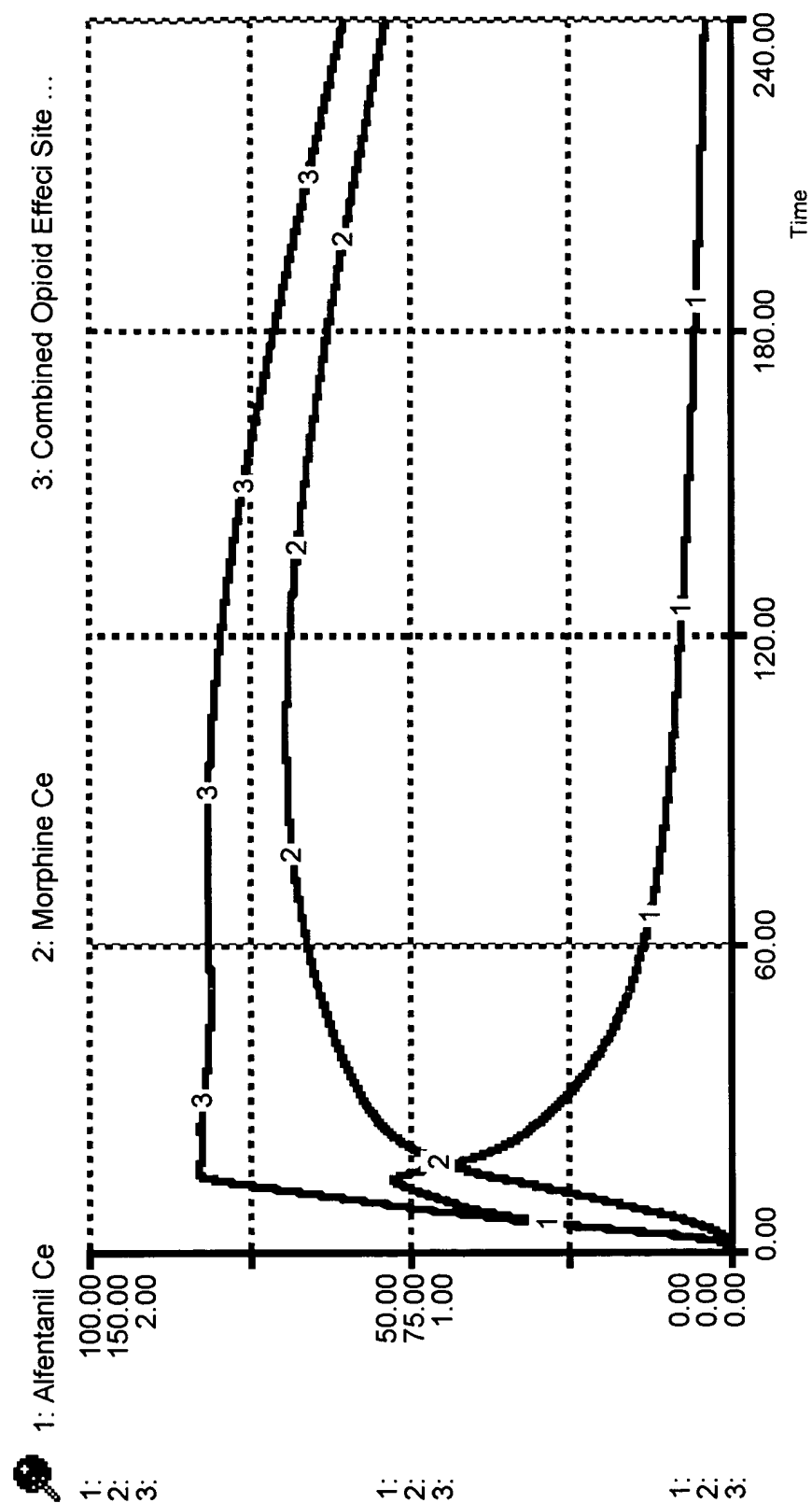
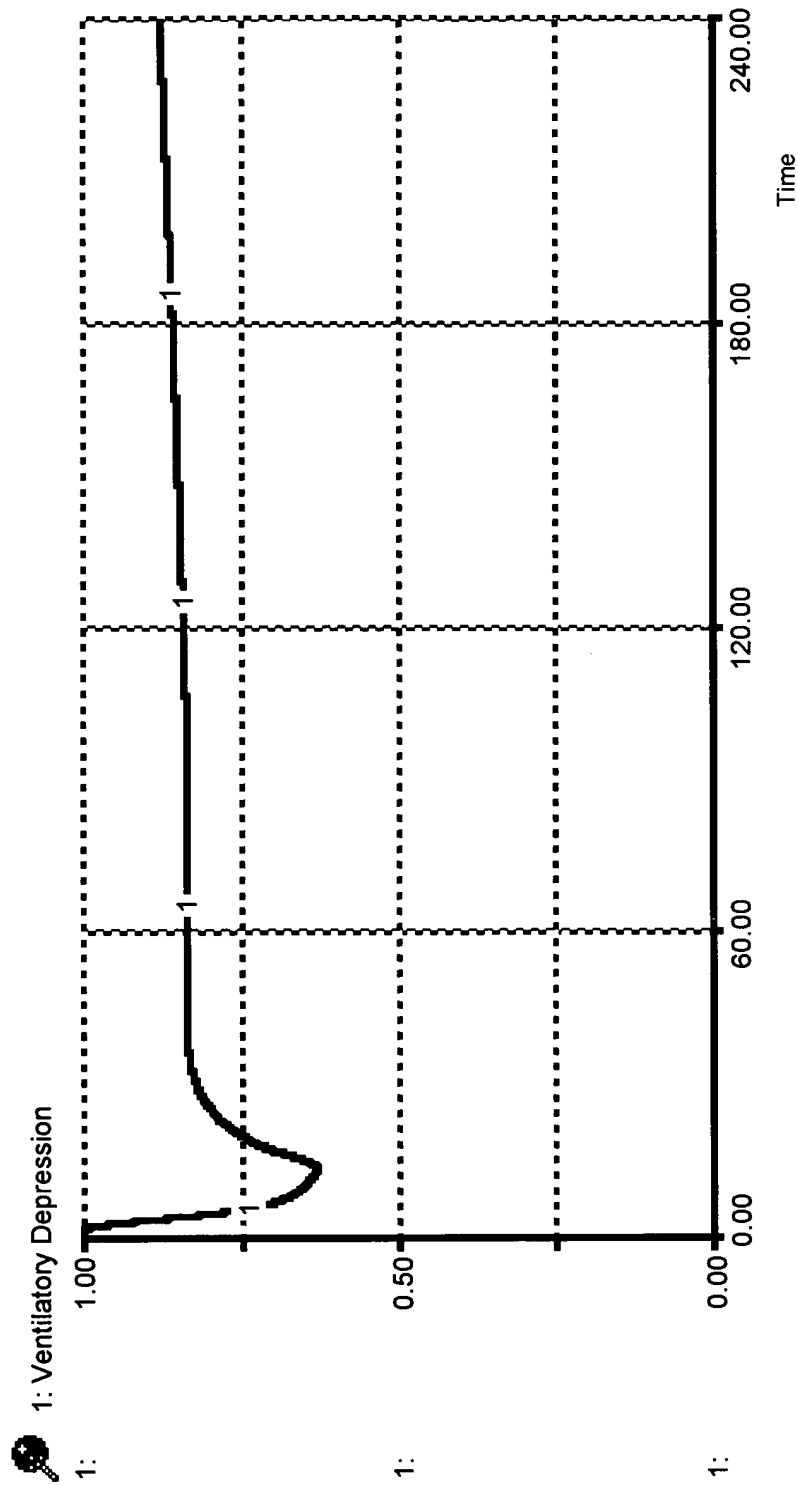


Figure 19



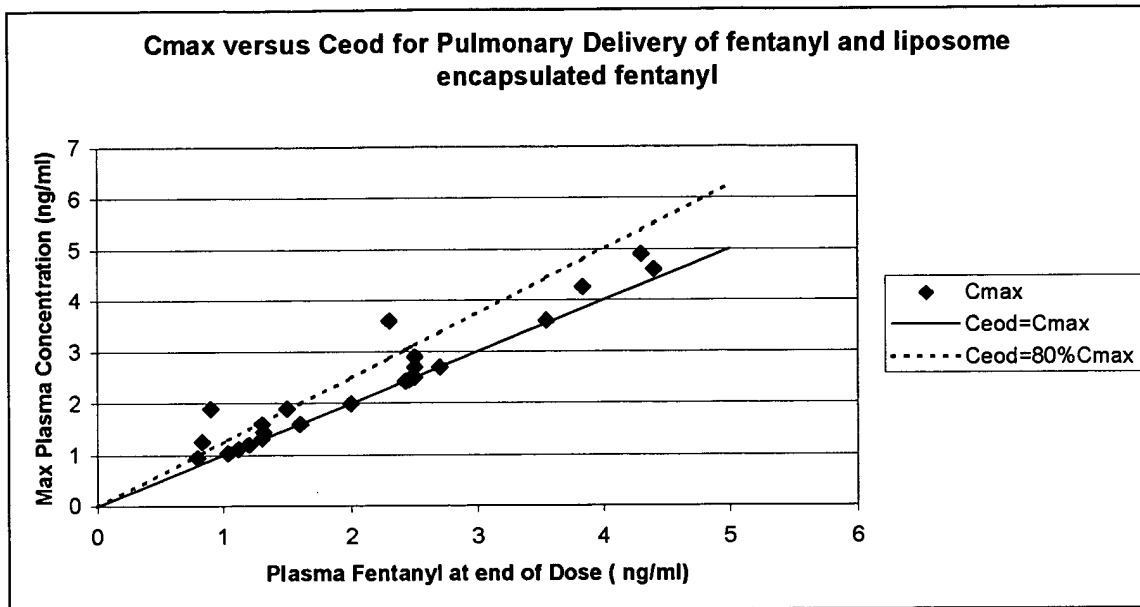


Figure 20A

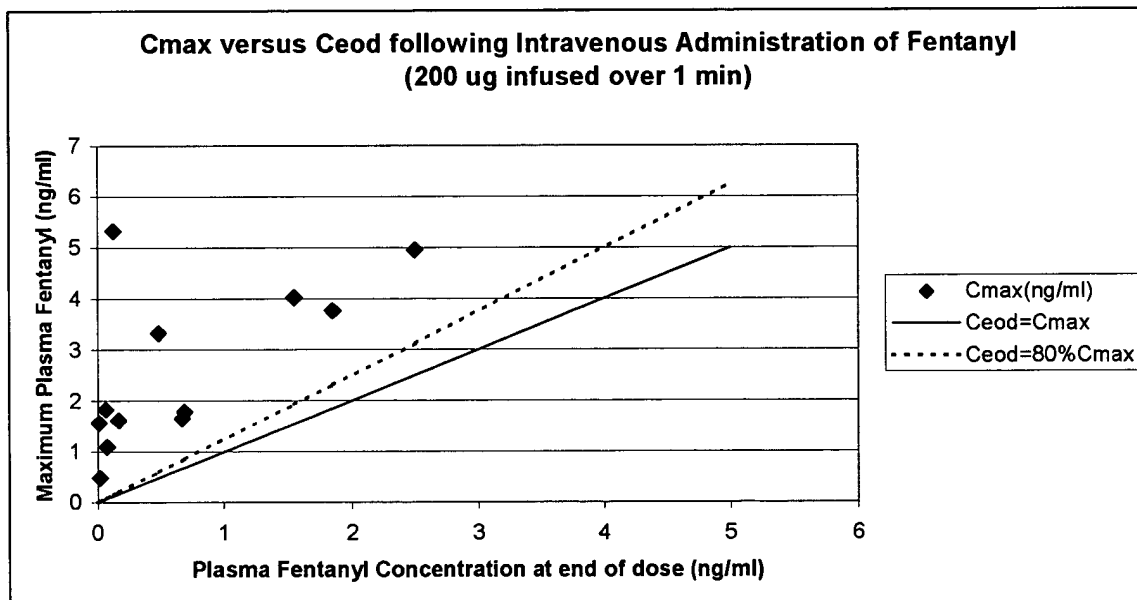


Figure 20B

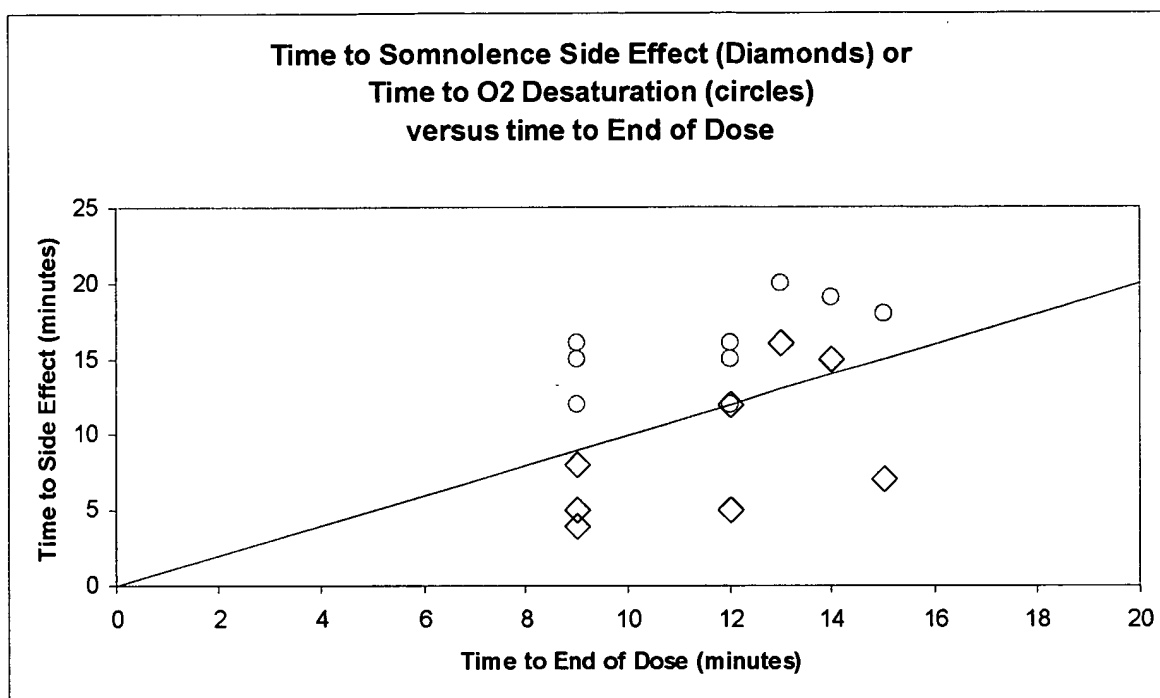


Figure 21

Figure 22: Correlation of side effect to toxic event

No side effect		Side effect	
N	26	24	
No hypoxia	22	14	36
Hypoxia	4	10	14
Null effect			
No hypoxia	18.72	17.28	36
Hypoxia	7.28	6.72	14
P value	0.038653124		